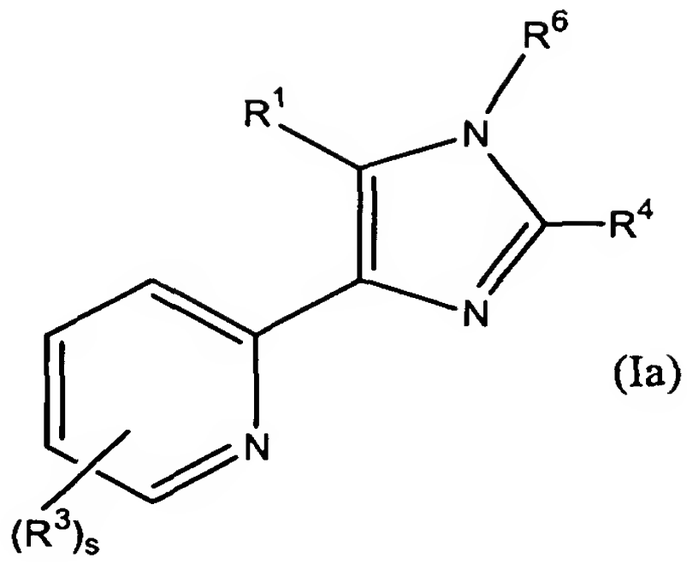
The claimed invention is:

1. A compound of formula (Ia):



(Ia)

or a pharmaceutically acceptable salt, prodrug, tautomer, hydrate, or solvate thereof, wherein:

$R^1$ is a saturated, unsaturated, or aromatic $C_3$-$C_{20}$ mono-, bi- or polycyclic ring optionally containing at least one heteroatom selected from the group consisting of N, O and S, wherein $R^1$ can optionally be further independently substituted with at least one moiety independently selected from the group consisting of: carbonyl, halo, halo($C_1$-$C_6$)alkyl, perhalo($C_1$-$C_6$)alkyl, perhalo($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_2$-$C_6$)alkynyl, hydroxy, oxo, mercapto, ($C_1$-$C_6$)alkylthio, ($C_1$-$C_6$)alkoxy, ($C_5$-$C_{10}$)aryl or ($C_5$-$C_{10}$)heteroaryl, ($C_5$-$C_{10}$)aryloxy or ($C_5$-$C_{10}$)heteroaryloxy, ($C_5$-$C_{10}$)ar($C_1$-$C_6$)alkyl or ($C_5$-$C_{10}$)heteroar($C_1$-$C_6$)alkyl, ($C_5$-$C_{10}$)ar($C_1$-$C_6$)alkoxy or ($C_5$-$C_{10}$)heteroar($C_1$-$C_6$)alkoxy, HO-(C=O)-, ester, amido, ether, amino, amino($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkylamino($C_1$-$C_6$)alkyl, di($C_1$-$C_6$)alkylamino($C_1$-$C_6$)alkyl, ($C_5$-$C_{10}$)heterocyclyl($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkyl- and di($C_1$-$C_6$)alkylamino, cyano, nitro, carbamoyl, ($C_1$-$C_6$)alkylcarbonyl, ($C_1$-$C_6$)alkoxycarbonyl, ($C_1$-$C_6$)alkylaminocarbonyl, di($C_1$-$C_6$)alkylaminocarbonyl, ($C_5$-$C_{10}$)arylcarbonyl, ($C_5$-$C_{10}$)aryloxycarbonyl, ($C_1$-$C_6$)alkylsulfonyl, and ($C_5$-$C_{10}$)arylsulfonyl;

each $R^3$ is independently selected from the group consisting of: hydrogen, halo, halo($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_2$-$C_6$)alkynyl, perhalo($C_1$-$C_6$)alkyl, phenyl, ($C_5$-$C_{10}$)heteroaryl, ($C_5$-$C_{10}$)heterocyclic, ($C_3$-$C_{10}$)cycloalkyl, hydroxy, ($C_1$-$C_6$)alkoxy, perhalo($C_1$-$C_6$)alkoxy, phenoxy,

($C_5$-$C_{10}$)heteroaryl-O-, ($C_5$-$C_{10}$)heterocyclic-O-, ($C_3$-$C_{10}$)cycloalkyl-O-, ($C_1$-$C_6$)alkyl-S-, ($C_1$-$C_6$)alkyl-$SO_2$-, ($C_1$-$C_6$)alkyl-NH-$SO_2$-, $O_2N$-, NC-, amino, $Ph(CH_2)_{1-6}HN$-, ($C_1$-$C_6$)alkyl HN-, ($C_1$-$C_6$)alkylamino, [($C_1$-$C_6$)alkyl]$_2$-amino, ($C_1$-$C_6$)alkyl-$SO_2$-NH-, amino(C=O)-, amino$O_2S$-, ($C_1$-$C_6$)alkyl-(C=O)-NH-, ($C_1$-$C_6$)alkyl-(C=O)-[(( ($C_1$-$C_6$)alkyl)-N]-, phenyl-(C=O)-NH-, phenyl-(C=O)-[( ($C_1$-$C_6$)alkyl)-N]-, ($C_1$-$C_6$)alkyl-(C=O)-, phenyl-(C=O)-, ($C_5$-$C_{10}$)heteroaryl-(C=O)-, ($C_5$-$C_{10}$)heterocyclic-(C=O)-, ($C_3$-$C_{10}$)cycloalkyl-(C=O)-, HO-(C=O)-, ($C_1$-$C_6$)alkyl-O-(C=O)-, $H_2N$(C=O)-, ($C_1$-$C_6$)alkyl-NH-(C=O)-, [($C_1$-$C_6$)alkyl]$_2$-N-(C=O)-, phenyl-NH-(C=O)-, phenyl-[(($C_1$-$C_6$)alkyl)-N]-(C=O)-, ($C_5$-$C_{10}$)heteroaryl-NH-(C=O)-, ($C_5$-$C_{10}$)heterocyclic-NH-(C=O)-, ($C_3$-$C_{10}$)cycloalkyl-NH-(C=O)- and ($C_1$-$C_6$)alkyl-(C=O)-O-;

where alkyl, alkenyl, alkynyl, phenyl, heteroaryl, heterocyclic, cycloalkyl, alkoxy, phenoxy, amino of $R^3$ is optionally substituted by at least one substituent independently selected from ($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, halo($C_1$-$C_6$)alkyl, halo, $H_2N$-, $Ph(CH_2)_{1-6}HN$-, and ($C_1$-$C_6$)alkylHN-;

s is an integer from one to five;

$R^4$ is independently selected from the group consisting of: hydrogen, halo, halo($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkyl, ($C_2$-$C_6$)alkenyl, ($C_2$-$C_6$)alkynyl, perhalo($C_1$-$C_6$)alkyl, phenyl, ($C_5$-$C_{10}$)heteroaryl, ($C_5$-$C_{10}$)heterocyclic, ($C_3$-$C_{10}$)cycloalkyl, hydroxy, ($C_1$-$C_6$)alkoxy, perhalo($C_1$-$C_6$)alkoxy, phenoxy, ($C_5$-$C_{10}$)heteroaryl-O-, ($C_5$-$C_{10}$)heterocyclic-O-, ($C_3$-$C_{10}$)cycloalkyl-O-, ($C_1$-$C_6$)alkyl-S-, ($C_1$-$C_6$)alkyl-S-($C_1$-$C_6$)alkyl-, ($C_1$-$C_6$)alkyl-$SO_2$-, ($C_1$-$C_6$)alkyl-NH-$SO_2$-, $O_2N$-, NC-, amino, aminoalkyl, $Ph(CH_2)_{1-6}HN$-, ($C_1$-$C_6$)alkylHN-, ($C_1$-$C_6$)alkylamino, [($C_1$-$C_6$)alkyl]$_2$-amino, ($C_1$-$C_6$)alkyl-$SO_2$-NH-, amino(C=O)-, amino$O_2S$-, ($C_1$-$C_6$)alkyl-(C=O)-NH-, ($C_1$-$C_6$)alkyl-(C=O)-(($C_1$-$C_6$)alkyl)-N-, phenyl-(C=O)-NH-, phenyl-(C=O)-[(($C_1$-$C_6$)alkyl)-N]-, ($C_1$-$C_6$)alkyl-(C=O)-, phenyl-(C=O)-, ($C_5$-$C_{10}$)heteroaryl-(C=O)-, ($C_5$-$C_{10}$)heterocyclic-(C=O)-, ($C_3$-$C_{10}$)cycloalkyl-(C=O)-, HO-(C=O)-, ($C_1$-$C_6$)alkyl-O-(C=O)-, $H_2N$(C=O)-, ($C_1$-$C_6$)alkyl-NH-(C=O)-, (($C_1$-$C_6$)alkyl)$_2$-N-(C=O)-, phenyl-NH-(C=O)-,

phenyl-[((C$_1$-C$_6$)alkyl)-N]-(C=O)-, (C$_5$-C$_{10}$)heteroaryl-NH-(C=O)-, (C$_5$-C$_{10}$)heterocyclic-NH-(C=O)-, (C$_3$-C$_{10}$)cycloalkyl-NH-(C=O)-, (C$_1$-C$_6$)alkyl-(C=O)-O-, (C$_1$-C$_6$)alkyl-(C=O)-NH-(C$_1$-C$_6$)alkyl, (C$_1$-C$_6$)alkyl-NH-(C=O)-(C$_1$-C$_6$)alkyl, and (C$_1$-C$_6$)alkyl-(C=O)-(C$_1$-C$_6$)alkyl;

where alkyl, alkenyl, alkynyl, phenyl, heteroaryl, heterocyclic, cycloalkyl, alkoxy, phenoxy, amino of $R^4$ is optionally substituted by at least one substituent independently selected from the group consisting of (C$_1$-C$_6$)alkyl, (C$_1$-C$_6$)alkoxy, halo(C$_1$-C$_6$)alkyl, halo, H$_2$N-, NC-, HO-, Ph (CH$_2$) $_{1-6}$HN-, (C$_1$-C$_6$)alkylHN-, (C$_5$-C$_{10}$)heteroaryl and (C$_5$-C$_{10}$)heterocyclyl;

$R^6$ is selected from the group consisting of hydrogen, (C$_1$-C$_6$)alkyl, (C$_2$-C$_6$)alkenyl, (C$_2$-C$_6$)alkynyl, phenyl, (C$_5$-C$_{10}$)heteroaryl, (C$_5$-C$_{10}$)heterocyclic, (C$_3$-C$_{10}$)cycloalkyl, (C$_1$-C$_6$)alkyl-(SO$_2$)-, (C$_1$-C$_6$)alkyl-(SO$_2$)-(C$_1$-C$_6$)alkyl, phenyl-(SO$_2$)-, H$_2$N-(SO$_2$)-, (C$_1$-C$_6$)alkyl-NH-(SO$_2$)-, (C$_1$-C$_6$)alkyl-(SO$_2$)-NH-(C$_1$-C$_6$)alkyl, (C$_1$-C$_6$)alkyl-NH-(SO$_2$)-(C$_1$-C$_6$)alkyl, ((C$_1$-C$_6$)alkyl)$_2$N-(SO$_2$)-, phenyl-NH-(SO$_2$)-, (phenyl)$_2$N-(SO$_2$)-, (C$_1$-C$_6$)alkyl-(C=O)-, (C$_1$-C$_6$)alkyl-(C=O)-(C$_1$-C$_6$)alkyl, phenyl-(C=O)-, (C$_5$-C$_{10}$)heteroaryl-(C=O)-, (C$_5$-C$_{10}$)heterocyclic-(C=O)-, (C$_3$-C$_{10}$)cycloalkyl-(C=O)-, (C$_3$-C$_{10}$)cycloalkyl-(C=O)-(C$_3$-C$_{10}$)cycloalkyl, (C$_1$-C$_6$)alkyl-O-(C=O)-, (C$_5$-C$_{10}$)heterocyclic-O-(C=O)-, (C$_3$-C$_{10}$)cycloalkyl-O-(C=O)-, H$_2$N-(C=O)-, (C$_1$-C$_6$)alkyl-NH-(C=O)-, (C$_1$-C$_6$)alkyl-NH-(C=O)-(C$_1$-C$_6$)alkyl, (C$_1$-C$_6$)alkyl-(C=O)-NH-(C$_1$-C$_6$)alkyl, phenyl-NH-(C=O)-, (C$_5$-C$_{10}$)heteroaryl-NH-(C=O)-, (C$_5$-C$_{10}$)heterocyclic-NH-(C=O)-, (C$_3$-C$_{10}$)cycloalkyl-NH-(C=O)-, (C$_3$-C$_{10}$)cycloalkyl-NH-(C=O)-(C$_3$-C$_{10}$)cycloalkyl, (C$_3$-C$_{10}$)cycloalkyl-(C=O)-NH-(C$_3$-C$_{10}$)cycloalkyl, ((C$_1$-C$_6$)alkyl)$_2$N-(C=O)-, (phenyl)$_2$N-(C=O)-, phenyl-[((C$_1$-C$_6$)alkyl)-N]-(C=O)-, (C$_5$-C$_{10}$)heteroaryl-[((C$_1$-C$_6$)alkyl)-N]-(C=O)-, (C$_5$-C$_{10}$)heterocyclic-[((C$_1$-C$_6$)alkyl)-N]-(C=O)-, and (C$_3$-C$_{10}$)cycloalkyl-[((C$_1$-C$_6$)alkyl)-N]-(C=O)-;

where alkyl, alkenyl, alkynyl, phenyl, benzyl, heteroaryl, heterocyclic, cycloalkyl, alkoxy, phenoxy, amino of $R^6$ is optionally substituted with at least one moiety independently selected from the group consisting of halo, $(C_1$-$C_6)$alkyl, $(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, perhalo$(C_1$-$C_6)$alkyl, $(C_3$-$C_{10})$cycloalkyl, phenyl, benzyl, $(C_5$-$C_{10})$heterocyclic, $(C_5$-$C_{10})$heteroaryl, $(C_1$-$C_6)$alkyl-$SO_2$-, formyl, NC-, $(C_1$-$C_6)$alkyl-(C=O)-, $(C_3C_{10})$cycloalkyl-(C=O)-, phenyl-(C=O)-, $(C_5$-$C_{10})$heterocyclic-(C=O)-, $(C_5$-$C_{10})$heteroaryl-(C=O)-, HO-(C=O)-, $(C_1$-$C_6)$alkyl-O-(C=O)-, $(C_3$-$C_{10})$cycloalkyl-O-(C=O)-, $(C_5$-$C_{10})$heterocyclic-O-(C=O)-, $(C_1$-$C_6)$alkyl-NH-(C=O)-, $(C_3$-$C_{10})$cycloalkyl-NH-(C=O)-, phenyl-NH-(C=O)-, $(C_5$-$C_{10})$heterocyclic-NH-(C=O)-, $(C_5$-$C_{10})$heteroaryl-NH-(C=O)-, $((C_1$-$C_6)$alkyl$)_2$-N-(C=O)-, phenyl-[$((C_1$-$C_6)$alkyl)-N]-(C=O)-, hydroxy, $(C_1$-$C_6)$alkoxy, perhalo$(C_1$-$C_6)$alkoxy, $(C_3$-$C_{10})$cycloalkyl-O-, phenoxy, $(C_5$-$C_{10})$heterocyclic-O-, $(C_5$-$C_{10})$heteroaryl-O-, $(C_1$-$C_6)$alkyl-(C=O)-O-, $(C_3$-$C_{10})$cycloalkyl-(C=O)-O-, phenyl-(C=O)-O-, $(C_5$-$C_{10})$heterocyclic-(C=O)-O-, $(C_5$-$C_{10})$heteroaryl-(C=O)-O-, $O_2N$-, amino, $(C_1$-$C_6)$alkylamino, $((C_1$-$C_6)$alkyl$)_2$-amino, formamidyl, $(C_1$-$C_6)$alkyl-(C=O)-NH-, $(C_3$-$C_{10})$cycloalkyl-(C=O)-NH-, phenyl-(C=O)-NH-, $(C_5$-$C_{10})$heterocyclic-(C=O)-NH-, $(C_5$-$C_{10})$heteroaryl-(C=O)-NH-, $(C_1$-$C_6)$alkyl-(C=O)-[$((C_1$-$C_6)$alkyl)-N]-, phenyl-(C=O)-[$(C_1$-$C_6)$alkyl-N]-, $(C_1$-$C_6)$alkyl-$SO_2$NH-, $(C_3$-$C_{10})$cycloalkyl-$SO_2$NH-, phenyl-$SO_2$NH-, $(C_5$-$C_{10})$heterocyclic-$SO_2$NH- and $(C_5$-$C_{10})$heteroaryl-$SO_2$NH-;

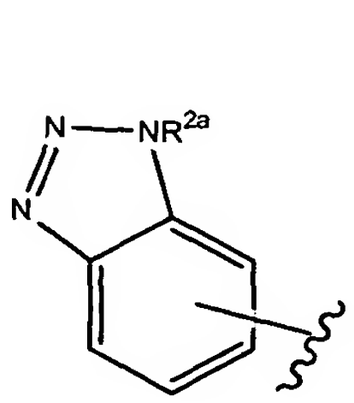
wherein the phenyl or heteroaryl moiety of a $R^6$ substituent is optionally further substituted with at least one radical independently selected from the group consisting of halo, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, perfluoro$(C_1$-$C_6)$alkyl and perfluoro$(C_1$-$C_6)$alkoxy,

with the proviso that when $R^4$ is a substituted phenyl group, then (a) $R^1$ is not a naphthyl, anthracenyl or phenyl and (b) if $R^1$ is a phenyl fused with an aromatic or non-aromatic cyclic ring of 5-7 members wherein said cyclic ring optionally contains up to three heteroatoms independently selected from N, O and S, then the fused cyclic ring of said $R^1$ moiety is substituted; and

with the proviso that when $R^4$ is hydrogen, then (a) $R^1$ is not a naphthyl or phenyl and (b) if $R^1$ is a phenyl fused with an aromatic or non-aromatic cyclic ring of 5-7 members wherein said cyclic ring optionally contains up to three heteroatoms independently selected from N, O and S, then the fused cyclic ring of said $R^1$ moiety is substituted; and

with the proviso that when $R^4$ is not hydrogen or substituted phenyl, then (a) $R^1$ is not a naphthyl, anthracenyl or phenyl and (b) if $R^1$ is a phenyl or pyridyl fused with an aromatic or non-aromatic cyclic ring of 5-7 members wherein said cyclic ring optionally contains up to three heteroatoms independently selected from N, O and S, and is optionally substituted by oxo, then the fused cyclic ring of said $R^1$ moiety contains at least one substituted heteroatom.

2. A compound of claim 1, wherein $R^1$ is



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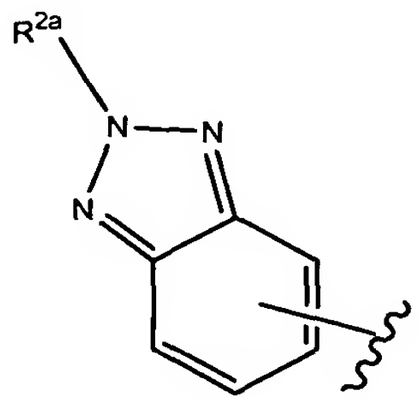
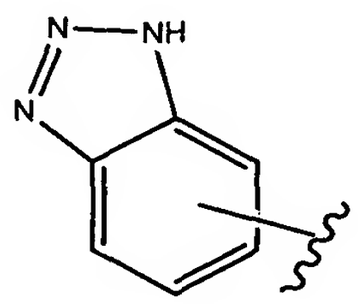


, or


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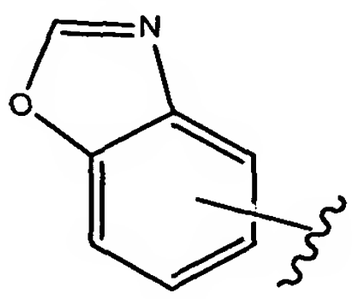
3. A compound of claim 1, wherein $R^1$ is



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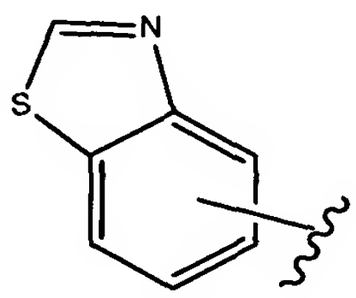

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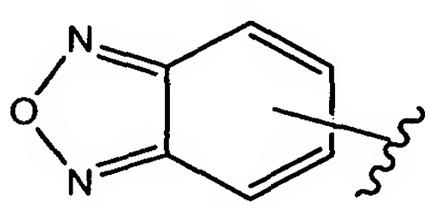

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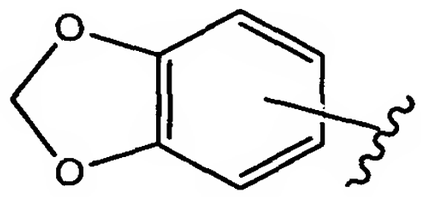
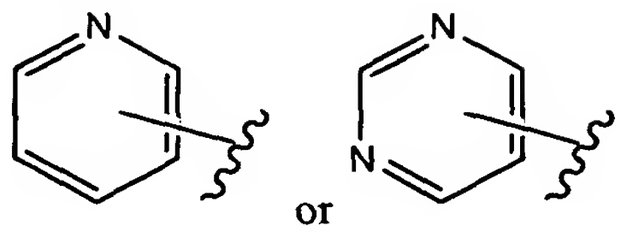


or .

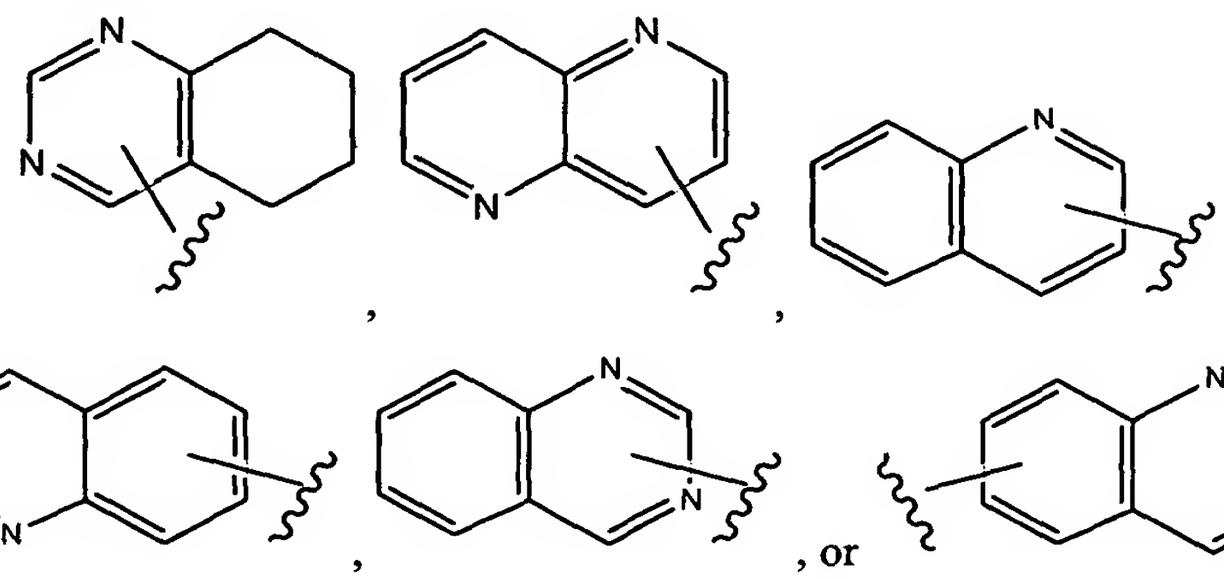
4. A compound of claim 1, wherein $R^1$ is



or

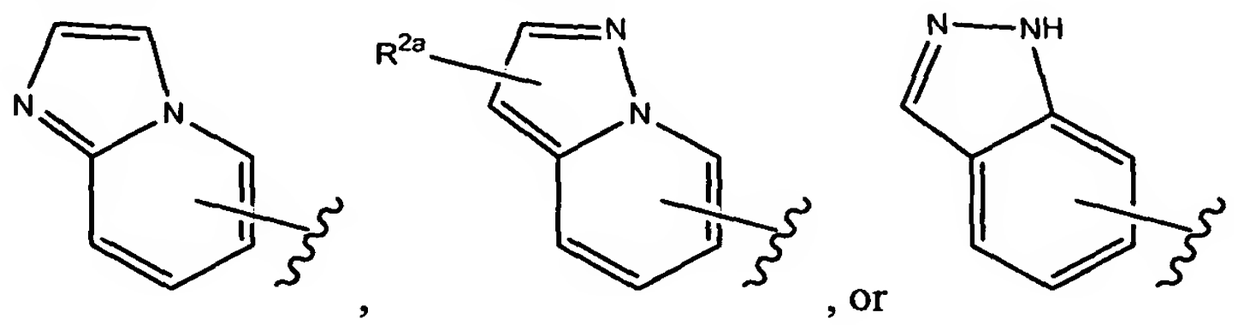
.

5. A compound of claim 1, wherein $R^1$ is



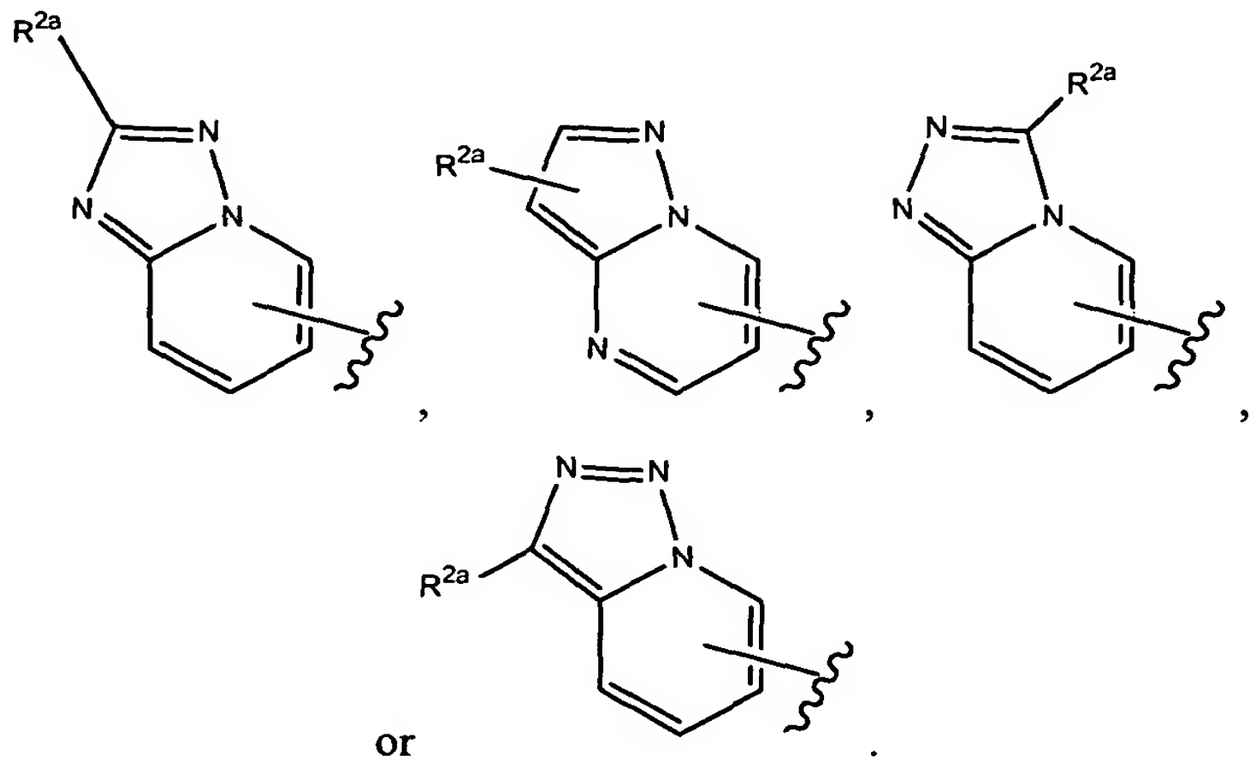
, or ..

6. A compound of claim 1, wherein $R^1$ is



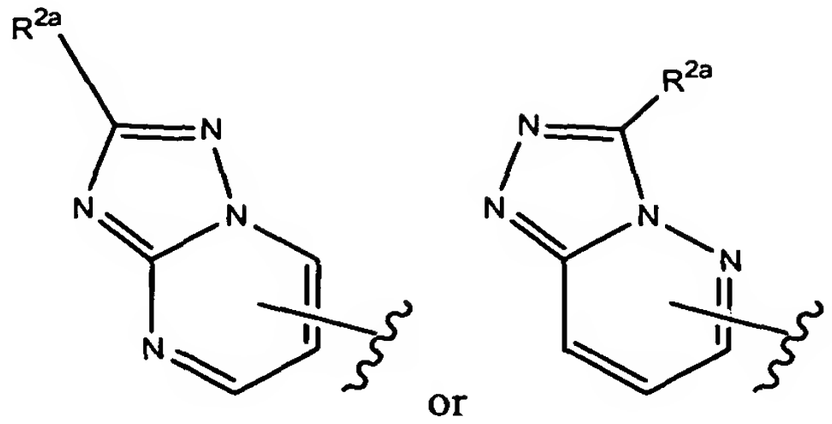
, or .

7. A compound of claim 1, wherein $R^1$ is



or .

8. A compound of claim 1, wherein $R^1$ is



or



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9. A compound of claim 1, wherein s is one to two; $R^3$ is hydrogen or ($C_1$-$C_6$)alkyl; $R^4$ is hydrogen, ($C_1$-$C_6$)alkyl, perhalo($C_1$-$C_6$)alkyl, phenyl, ($C_1$-$C_6$)alkyl-S-($C_1$-$C_6$)alkyl-, ($C_5$-$C_{10}$)heteroaryl, ($C_3$-$C_{10}$)cycloalkyl, aminoalkyl, amino(C=O)-, ($C_1$-$C_6$)alkyl-(C=O)-NH-($C_1$-$C_6$)alkyl, or ($C_1$-$C_6$)alkyl-NH-(C=O)-($C_1$-$C_6$)alkyl; and $R^6$ is H, ($C_1$-$C_6$)alkyl, ($C_3$-$C_{10}$)cycloalkyl, ($C_1$-$C_6$)alkyl-($SO_2$)-($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkyl-($SO_2$)-NH-($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkyl-NH-($SO_2$)-($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkyl-(C=O)-($C_1$-$C_6$)alkyl, ($C_3$-$C_{10}$)cycloalkyl-(C=O)-($C_3$-$C_{10}$)cycloalkyl, ($C_1$-$C_6$)alkyl-NH-(C=O)-($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkyl-(C=O)-NH-($C_1$-$C_6$)alkyl, ($C_3$-$C_{10}$)cycloalkyl-NH-(C=O)-($C_3$-$C_{10}$)cycloalkyl, or ($C_3$-$C_{10}$)cycloalkyl-(C=O)-NH-($C_3$-$C_{10}$)cycloalkyl.

10. A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.

11. A method of preventing or treating a TGF-related disease state in an animal or human comprising the step of administering a therapeutically effective amount of a compound of claim 1 to the animal or human suffering from the TGF-related disease state.

12. A method of claim 11, wherein said TGF-related disease state is selected from the group consisting of cancer, glomerulonephritis, diabetic nephropathy,

hepatic fibrosis, pulmonary fibrosis, intimal hyperplasia and restenosis, scleroderma, and dermal scarring.

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